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US 4794171	USP 19881227	11
US 4222128	USP 19800916	5

# United States Patent Chow et al.

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## [54] SELF-SETTING CALCIUM PHOSPHATE CEMENTS AND METHODS FOR PREPARING AND USING THEM

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[73] Assignee: American Dental Association Health Foundation, Gaithersburg, Md.

[\*] Notice: This patent is subject to a terminal disclaimer.

[21] Appl. No.: 08/846,145

[22] Filed: Apr. 25, 1997

### Related U.S. Application Data

[60] Continuation of application No. 08/478,670, Jun. 7, 1995, abandoned, which is a division of application No. 08/126,502, Sep. 24, 1993, Pat. No. 5,525,148

[51] Int. Cl.<sup>5</sup> C09K 3/00

[52] U.S. Cl. 106/35; 106/69; 106/691; 106/792; 623/16; 433/201.1

[58] Field of Search 106/35, 690, 691, 106/692; 623/16; 433/201.1

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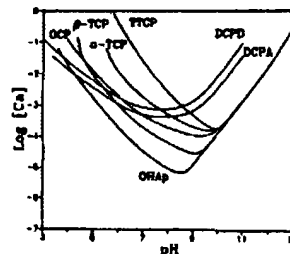
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### [57]

### ABSTRACT

The invention includes methods and compositions relating to calcium phosphate cements, which self-harden substantially to hydroxyapatite at ambient temperature when in contact with an aqueous medium. More specifically the cements comprise a combination of one or more sparingly soluble calcium phosphates other than tetracalcium phosphate with an aqueous solution adjusted with a base to maintain a pH of about 12.5 or above and having sufficient dissolved phosphate salt to yield a solution mixture with phosphate concentration equal to or greater than about 0.2 mol/L.

22 Claims, 1 Drawing Sheet



EAST search 3/29/01  
best art

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7	US 4222128	USP:19800916	5	Com

(12) **United States Patent**  
Brown et al.

(10) Patent No.: **US 6,201,039 B1**  
(45) Date of Patent: **\*Mar. 13, 2001**

(54) **BONE SUBSTITUTE COMPOSITION  
COMPRISING HYDROXYAPATITE AND A  
METHOD OF PRODUCTION THEREFOR**

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(73) Assignee: The Penn State Research Foundation, University Park, PA (US)

(\*) Notice: This patent issued on a continued prosecution application filed under 37 CFR 1.53(d), and is subject to the twenty year patent term provisions of 35 U.S.C. 154(a)(2).

Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 00 days.

(21) Appl. No.: 08/617,809

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**Related U.S. Application Data**

(63) Continuation-in-part of application No. 08/124,731, filed on Sep. 21, 1993, now abandoned.

(51) Int. Cl. A61F 2/28

(52) U.S. Cl. 523/115; 424/423

(56) Field of Search 424/423; 523/115, 523/116

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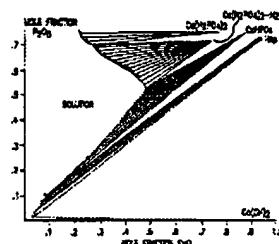
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(57) **ABSTRACT**

The present invention is directed to polymineralic particles which are precursors of hydroxyapatite and a method for their production. The present invention is also directed to a synthetic bone-like composition comprising said hydroxyapatite polymineralic precursor particles of hydroxyapatite and optionally, a polymeric material capable of promoting mineralization of hydroxyapatite, which are useful for fixing prosthetic devices, useful as bone substitutes to directly fill bone defects, to provide substrates for cartilage, and to repair teeth, and methods of making such preparations. The present invention is also directed to a method of treating collagen to provide a micro-structure close to that of native bone.

22 Claims, 5 Drawing Sheets



THE PRESENT INVENTION IS DIRECTED TO POLYMINERALIC PARTICLES WHICH ARE PRECURSORS OF HYDROXYAPATITE AND A METHOD FOR THEIR PRODUCTION.